With this response, claims 1-9 and 16 are now pending. Applicants do not believe that any fees are due at this time; however, should any fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason relating to this document, the Commissioner is authorized to deduct the fees from Howrey Simon Arnold & White Deposit Account No. 08-3038.

For the Examiner's convenience, a list of currently pending claims is attached at the end of this document.

I. Restriction Requirement

With respect to the prior restriction requirement, the Examiner acknowledges the election of group I, claims 1-10, with traverse. However, the Examiner rejects the grounds for traverse and makes the restriction requirement final. The Examiner also notes the election of SEQ ID NOS:1-10 and requires (by way of rejection under 35 U.S.C. §112, 2nd paragraph) that the claims be amended commensurate in scope with the elected sequences. While Applicants disagree with the restriction and election requirements, to facilitate prosecution they have amended the claims accordingly.

II. Specification

The Examiner notes the incorporation of embedded hyperlinks on pages 1, 2, and 6 of the specification. According to MPEP §608.01, embedded hyperlinks and browser executable code are not permitted. The specification has been amended to remove the phrase "http://."

The Examiner further suggests that these website addresses are improperly incorporated by reference. Applicants disagree. The websites have not been incorporated by reference. Rather, the website addresses are provided as sources of additional guidance and background material for one of skill in the art. Significantly, Applicants note that none of the

website addresses are followed by the phrase, "herein incorporated by reference." *See*, e.g., specification as filed at page 1, line 23, page 4, lines 18-21, page 29, line 22, page 60, line 5, and page 89, line 22. References that Applicants have intended to incorporate by reference are consistently followed by this phrase throughout the application. In view of the above, Applicants request that the objection to the specification be withdrawn.

III. Rejections under 35 U.S.C. §112, 2nd Paragraph

Claims 1-10 were rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. With respect to claims 1-7, the Examiner contends that the term "specifically" is unclear. Applicants disagree. The term "specifically" is defined in the specification at, for example, page 14, lines 1-3. Nevertheless, to facilitate prosecution applicants have amended claims 1-7 to recite specific hybridization conditions.

In addition, the Examiner contends that claims 9-10 are indefinite for recitation of the phrase "nucleic acid molecules having one or two of said defined ends." Applicants disagree. The phrase "defined ends" is a well-known term of art, and is used in the specification interchangeably with the term "sequence tagged connectors" or STCs, another well-known term of art. *See* specification at, for example, page 1, lines 15-27, page 9, lines 3-5, and page 13, line 20 to page 14 line 22. However, to facilitate prosecution, Applicants have replaced the phrase "defined ends" with specific sequence ID numbers.

IV. Rejection under 35 U.S.C. §101

Claims 1-10 were rejected under 35 U.S.C. §101, because the claimed invention is allegedly not supported by either a substantial and/or specific, or well-established utility as

outlined in the Revised Interim Utility Guidelines Training Materials ("Interim Training Guidelines").

The Examiner acknowledges that the specification describes multiple utilities for the present invention, including "probes or markers for assisting in the isolation of full-length cDNAs or genes which would be used to make protein and optionally further usage to isolate of [sic] homologous sequences, molecular weight markers, chromosomal markers, and for numerous other generic genetic engineering usages." Office Action dated September 12, 2000, at pages 6-7. However, the Examiner contends that none of these utilities constitute a "substantial" or "specific" utility as defined in the Interim Training Guidelines.

Applicants traverse this rejection. The Examiner's application of these Interim Training Guidelines ignores the presently disclosed utilities and contravenes well-established doctrines of utility developed in the courts.

It is well-established law that "when a properly claimed invention meets at least one stated objective, utility under section 101 is clearly shown." *Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 958, 220 U.S.P.Q. 592, 598 (Fed. Cir. 1983). As acknowledged by the Examiner, the specification describes multiple objectives and utilities. For example, the invention is useful for determining the presence and/or identity of polymorphisms, measuring the level of an mRNA in a sample, determining the location of a corresponding DNA sequence on a physical or genetic map, obtaining other nucleic acid molecules from the same species, obtaining related protein coding sequences, obtaining promoters and other flanking genetic elements to such molecules, screening cDNA or genomic libraries, obtaining nucleic acid homologues, detecting and characterizing gene expression, probing for other molecules, generating primers, *etc.* (*see e.g.*, Specification, beginning at page 35, under heading "Uses of the Agents of the Invention").

Many of these uses are directly analogous to the use of a microscope. An important utility of a microscope resides in its use to identify and characterize the structure of biological tissues in a sample, cell, or organism. Significantly, the utility of a microscope under 35 U.S.C. §101 is not compromised by its use as a tool in this manner. Many of the presently disclosed utilities are directly analogous to the utilities of a microscope, *i.e.*, the claimed nucleic acid molecules may be used to identify and characterize nucleic acid molecules within a sample, cell, or organism. Such utility is indistinguishable from the legally sufficient utility of a microscope. Thus, the presently disclosed sequences possess the requisite utility under 35 U.S.C. §101.

In the Office Action, the Examiner provides no evidence challenging the disclosed utilities for the presently claimed nucleic acid molecules. Rather, the Examiner attempts to undermine the existing utilities by stating ". . . the disclosed uses . . . are not specific and are generally applicable to any nucleic acid." Office Action dated September 12, 2000, at page 6. Further, ". . . utilities . . . in the instant specification are neither substantial nor specific due to being generic in nature and application to a myriad of such compounds." *Id.* at page 7. In short, the Examiner suggests that the asserted utilities are legally insufficient simply because other molecules can be used for the same purpose. This position is wrong as a matter of law - there is no requirement of exclusive utility in the patent law. *See Carl Zeiss Stiftung v. Renishaw PLC*, 945 F2d 1173, 1180, 20 U.S.P.Q.2d 1094, 1100 (Fed. Cir. 1991) ("An invention need not be the best or the only way to accomplish a certain result...").

Moreover, this position offends the sensibilities. For example, such an argument implies that a new golf club has no legal utility because other golf clubs can be used for the same purpose, *i.e.*, hitting golf balls. Such a result is not only untenable, but requires reading "into the patent laws limitations and conditions which the legislature has not expressed," a

practice condemned by the Supreme Court. *See Diamond v. Chakrabarty*, 447 U.S. 303, 308, 206 U.S.P.Q. 193, 196 (1980), *quoting United States v. Dubilier Condenser Corp.*, 289 U.S. 178, 199, 17 U.S.P.Q. 154, 162 (1933). Thus, it must be the case that an utility, generic to a broad class of molecules, does not compromise the specific utility of an individual member of that class.

Applicants note that the claimed nucleic acid molecules encompass many utilities. Some of these utilities may be common to a broader class of molecules. For instance, nucleic acid sequences may generally be used to identify and isolate related sequences. However, when used in this manner, the result is not generic. Rather, the claimed nucleic acid molecules will identify a ***unique*** subset of related sequences. This subset of related sequences is specific to the claimed sequences and cannot be identified by any generic nucleic acid molecule. For example, a random nucleic acid molecule would not provide this specific utility. Referring again to the golf club analogy, the club is still generically hitting a golf ball, but is uniquely designed to hit the ball in a manner that is distinct from other clubs. Once again, Applicants assert that the claimed nucleic acid sequences exhibit the requisite utility under 35 U.S.C. §101.

Surprisingly, the Examiner contends that the credibility of the presently asserted utilities has not been assessed. Office Action dated September 12, 2000, at page 7. This is precisely the issue that the courts have emphasized in evaluating the adequacy of an asserted utility. Utility is determined "by reference to, and a factual analysis of, the disclosure of the application." *In re Ziegler*, 992 F.2d 1197, 1201, 26 U.S.P.Q.2d 1600, 1603 (Fed. Cir. 1993), *quoting Cross v. Iizuka*, 753 F.2d 1040, 1044, 224 U.S.P.Q. 739, 742 (Fed. Cir. 1985). The Examiner "has the initial burden of challenging a presumptively correct assertion of utility in the disclosure." *In re Brana*, 51 F.3d 1560, 1567, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir.

1995). The utilities asserted in the specification must be accepted as factually sound unless the Patent Office cites information that undermines the credibility of the assertion. *Id.* The Examiner "must do more than merely question operability – [he] must set forth factual reasons which would lead one skilled in the art to question the objective truth of the statement of operability." *In re Gaubert*, 524 F.2d 1222, 1225-26, 187 U.S.P.Q. 664, 666 (C.C.P.A. 1975) (emphasis in original); MPEP § 706.03(a)(1) ("Office personnel are reminded that they must treat as true a statement of fact made by an applicant in relation to an asserted utility, unless countervailing evidence can be provided...").

Here, the Examiner has not even attempted to meet this burden. Thus, the Examiner's admission that the credibility of the disclosed utilities is not challenged is tantamount to an admission that no proper rejection has been made.

In view of the above, Applicants contend that the claimed nucleic acid molecules are supported by credible, specific, and substantial utilities disclosed in the specification. Moreover, the Examiner has failed to raise any credible evidence challenging the presently asserted utilities. Consequently, the rejection of claims 1-10 under 35 U.S.C. §101 is incorrect and should be withdrawn.

V. Rejection under 35 U.S.C. §112, 1st Paragraph: Enablement

Claims 1-10 were rejected under 35 U.S.C. § 112, first paragraph, as not being enabled by the specification, because the claimed invention allegedly lacks utility (*i.e.* an invention with no utility cannot be enabled). This rejection has been overcome by the foregoing arguments regarding utility.

Moreover, the Examiner has not met the evidentiary burden required to impose an enablement rejection. A specification that discloses how to use the claimed invention "must

be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein." *In re Brana*, 51 F.3d 1560, 1566, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995), *quoting In re Marzocchi*, 439 F.2d 220, 223, 169 U.S.P.Q. 367, 369 (C.C.P.A. 1971) (emphasis in original). It is also well-established law that "the enablement requirement is met if the description enables any mode of making and using the invention." *Johns Hopkins University v. CellPro*, 152 F.3d 1342, 1361, 47 U.S.P.Q.2d 1705, 1719 (Fed. Cir. 1998) (emphasis added), *quoting Engel Indus. v. Lockformer Co.*, 946 F.2d 1528, 1533, 20 U.S.P.Q.2d 1300, 1304 (Fed. Cir. 1991).

As discussed above, the present specification discloses how to use the claimed nucleic acid molecules (*e.g.*, identifying the presence or absence of a polymorphism, measuring the level of an mRNA in a sample, determining the location of a corresponding DNA sequence on a physical or genetic map, probing for other molecules, generating primers, *etc.*). The Examiner, however, has provided neither evidence supporting the rejection, nor any explanation of why the specification allegedly fails to enable such uses. *See In re Wright*, 999 F.2d 1557, 1561-62, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993); *Ex parte Lemak*, 210 U.S.P.Q. 306, 307 (Bd. App. 1981) ("pure conjecture" does not substantiate rejection for lack of enablement).

Thus, the enablement rejection under 35 U.S.C. § 112, first paragraph, is incorrect and should be withdrawn.

VI. Rejection under 35 U.S.C. §112, 1st Paragraph: Written Description

Claims 1-10 were rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in a manner that reasonably conveys to one of ordinary skill in the art that the inventors had possession of the

claimed invention at the time of filing. The Examiner admits that claims directed to SEQ ID NOS: 1-10 satisfy the enablement and written description provisions of §112. However, the Examiner rejects the claims "directed to encompass gene sequences (that could include any microsatellite sequences, single polynucleotide polymorphism, etc), sequences that hybridize to SEQ ID NO:1-10, or fragment thereof, which would include sequences from other species, mutated sequences, allelic variants, splice variants, fragments of those sequences, and so forth." Office Action dated September 12, 2000, at page 8. Thus, the Examiner contends that the specification does not provide sufficient written description to support the genus encompassed by the claims. Applicants respectfully disagree.

As the Examiner notes, the purpose of the written description requirement is to ensure that the inventors had possession of the claimed subject matter, *i.e.*, to ensure that the inventors actually invented what is claimed. *Gentry Gallery Inc. v. Berkline Corp.*, 134 F.3d 1473, 1479, 45 U.S.P.Q.2d 1498, 1503 (Fed. Cir. 1998); *Lockwood v. American Airlines*, 107 F.3d 1565, 1572, 41 U.S.P.Q.2d 1961, 1966 (Fed. Cir. 1997); *In re Alton*, 76 F.3d 1168, 1172, 37 U.S.P.Q.2d 1578, 1581 (Fed. Cir. 1996). In accordance with this purpose, Applicants need not "describe," in the sense of Section 112, all things that are encompassed by the claims. To contend otherwise would contradict established jurisprudence, which teaches that a patent may be infringed by technology developed after a patent issues. *United States Steel Corp. v. Phillips Petroleum Co.*, 865 F.2d 1247, 1251, 9 U.S.P.Q.2d 1461, 1464 (Fed. Cir. 1989). A related, and equally well-established principle of patent law is that claims "may be broader than the specific embodiment disclosed in a specification." *Ralston Purina Co. v. Far-Mar-Co*, 772 F.2d 1570, 1575, 227 U.S.P.Q. 177, 179 (Fed. Cir. 1985), *quoting In re Rasmussen*, 650 F.2d 1212, 1215, 211 U.S.P.Q. 323, 326 (C.C.P.A. 1981). Thus, simply because the claimed nucleic acid sequences may also include sequences from other species,

mutated sequences, allelic variants, splice variants, etc. does not require that Applicants describe each and every one of these molecules.

The Examiner further contends that the skilled artisan cannot envision the detailed chemical structure of the claimed polynucleotides and/or proteins. According to the Examiner, proper written description support for a claim directed to a nucleic acid sequence requires nothing less than the actual disclosure of every sequence encompassed by that claim. In support of this proposition, the Examiner relies on *Regents of the University of California v. Eli Lilly and Co,* 119 F.3d 1559, 43 U.S.P.Q.2d 1398, (Fed. Cir. 1997).

Applicants respectfully disagree. In *Eli Lilly* the court found that claims to a vertebrate cDNA encoding insulin were inadequately described. However, the present case is clearly different. Specifically, the present claims "distinguish the claimed genus from others" and define "structural features commonly possessed by members of the genus that distinguishes them from others," unlike the claims at issue in *Eli Lilly*. *Id.* at 1568-69 ("a cDNA is not defined or described by the mere name 'cDNA'...but requires a kind of specificity usually achieved by means of the recitation of the sequence of nucleotides that make up the DNA.").

In particular, Applicants have provided a detailed chemical structure, *i.e.*, the nucleic acid sequence of SEQ ID NOS:1-10. Moreover, closely related nucleic acid molecules falling within the scope of the present claims are readily identifiable – they either hybridize under the claimed conditions to SEQ ID NOS:1-10 (or complements thereof) or they do not. The fact that the nucleic acid molecules may comprise additional sequences or variations is beside the point. Such modifications are readily envisioned by one of ordinary skill in the art and disclosed throughout the present specification. Thus, there is no deficiency in the written description support for the present claims.

In view of the above, Applicants request that the rejection of claims 1-6 under 35 U.S.C. § 112, first paragraph, be withdrawn.

VII. Rejection under 35 U.S.C. §102

Claims 1 and 4 were rejected under: 35 U.S.C. §102(a) as allegedly being anticipated by Liu (WO 99/10535) or Imsande (Examiner's Sequence Homology Search); 35 U.S.C. §102(b) as allegedly being anticipated by Larkins (U.S. Patent No. 5,824,523), Lindsay (Examiner's Sequence Homology Search), Shoemaker (Examiner's Sequence Homology Search), Waterston (Examiner's Sequence Homology Search), Laten (Examiner's Sequence Homology Search), Elder (U.S. Patent No. 5,736,378), and Nakamura (Examiner's Sequence Homology Search); and 35 U.S.C. §102(e) as allegedly being anticipated by Moineau (US 4,886,878).

A rejection under 35 U.S.C. 102(b) is proper if, *inter alia*, an anticipatory printed publication describes the invention more than one year prior to Applicants' effective filing date.

With respect to §102(b), the Lindsay, Shoemaker, Waterston, and Nakamura references cited by the Examiner appear to have been published after, or less than one year prior to, Applicants' filing date. Applicants presently claim a filing date of October 15, 1999. The dates assigned by the Examiner to each of the sequence database entries are erroneous. For each database entry, the Examiner appears to rely on the date that the sequence was submitted to the database. However, these submission dates do not correspond with the date a sequence was published and publicly accessible via the database. Thus, such submission dates are insufficient to support a rejection under §102 because none of the references were

"printed publications" as of Applicants' effective filing date. Therefore, these four references are not prior art for the purposes of §102(b).

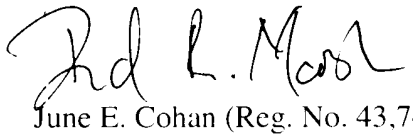
However, even if all of the references cited by the Examiner were valid as prior art, none of the references anticipate the present claims. For a prior art reference to anticipate in terms of 35 U.S.C. § 102, every element of the claimed invention must be identically shown in a single reference. *Diversitech Corp. v. Century Steps, Inc.*, 850 F.2d 675, 677, 7 U.S.P.Q.2d 1315, 1317 (Fed. Cir. 1988). Applicants contend that none of these references teach every element of the claimed invention.

The Examiner has asserted that Moineau anticipates claims 1 and 4 (35 U.S.C. § 102(e)). The presently amended claims recite "hybridizing, under conditions of 6.0 x sodium chloride/sodium citrate (SSC) at about 45°C, followed by a wash of 2.0 x SSC at 50°C." The Moineau sequence has only 21.4% identity to SEQ ID NO: 1. It will not hybridize to SEQ ID NO: 1 under the presently claimed conditions. Moreover, the small region of homology cited by the Examiner (66 basepairs having 66.7% identity) is clearly insufficient to permit hybridization of the entire Moineau sequence (2984 total basepairs having only 21.4% identity). Consequently, Moineau does not teach all of the elements of the present claims.

None of the sequences in the references cited by the Examiner anticipate the claimed sequences under the conditions recited in the presently amended claims. Therefore, none of the cited references teach all of the elements of the claimed invention. Accordingly, Applicants respectfully request that the rejections of claims 1 and 4 under 35 U.S.C. §102(b) and (e) be withdrawn.

The Examiner is encouraged to contact the undersigned should any additional information be necessary for allowance.

Respectfully submitted,



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